REMARKS

Reconsideration of the above-identified application in view of the amendment above and the remarks below is respectfully requested.

No claims have been canceled or added in this paper. Claim 1 has been amended in this paper. Therefore, claims 1-12, 14-18, 20-23, 25-26, 30-34, 36 and 41 are pending and are under active consideration.

Claims 1-12, 14-18, 20-23, 25-26, 30-34, 36 and 41 stand rejected under 35 U.S.C. 112, first paragraph "as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." In support of the rejection, the Patent Office states the following:

> The claims are drawn to a diagnostic or therapeutic method comprising determining genes that have differences in expression and methylation by comparison of two cancerous biological samples. The specification describes a method of determining genes that have differences in expression and methylation relative to two groups of samples on page 11, relative to healthy and/or diseases samples on page 12, and relative to prostate cancer cell lines and healthy prostate cells on page 21. The specification does not describe a diagnostic or therapeutic method of determining genes that have differences in expression and methylation by comparison of two cancerous biological samples.
>
> Applicant's arguments filed 17 July 2008 have been fully considered but they are not persuasive. The applicants point to the paragraph bridging pages 21-22 for support of a diagnostic or therapeutic method of determining genes that have differences in expression and methylation by comparison of two cancerous

> biological samples. The cited passage states "at least one biological sample is derived from biological material of healthy and/or diseased individuals." This recitation does not describe a comparison of two samples, both of which are cancerous. The applicants point to the term "and/or" as supporting the claimed subject matter, but the passage as a whole does not indicate that both samples are cancerous and the rejection is maintained.

Applicants respectfully traverse the subject rejection. As best understood by Applicants, the subject rejection appears to be predicated on the recitation in claim 1 that each of the at least two groups is cancerous. Without acquiescing in the propriety of the rejection, Applicants note that claim 1 has been amended in such a way that the language in question is no longer recited.

Therefore, the subject rejection is moot and should be withdrawn.

Claims 1-12, 14-18, 20-23, 25-26, 30-34, 36 and 41 stand rejected under 35 U.S.C. 112, first paragraph, "as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." In support of the rejection, the Patent Office states the following:

> In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.
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> In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must use a diagnostic or therapeutic method of determining genes that have differences in expression and methylation by comparison of two cancerous biological samples. For the reasons discussed below there would be an unpredictable amount of experimentation required to make the claimed invention.

b) The specification presents guidance on pages 14-18 to compare healthy and diseased samples.

c) The specification presents a working example on page 21 of comparison of prostate cancer cell line cells to healthy prostate cells.

d) The nature of the invention, molecular diagnostic assays, is complex.

e) Huang et al. shows a method of determining methylation sites relevant to breast cancer. Huang et al. shows in the abstract and throughout that the comparison was done between breast cancer cells and **normal** tissue so that differences that correlate with breast cancer could be determined.

f) The skill of those in the art of molecular diagnostic assays is high.

g) It is predictable from prior art such as Huang et al. that qualities of cancerous samples that are relevant to disease for diagnostic or therapeutic purposes should be compared to normal tissue controls so that the changes are known to appear only in diseased tissue.

h) The claims are broad in that they require determination of gene panels useful for diagnostic or therapeutic purposes to be determined without determining whether the gene panels contain genes whose expression and methylation levels correlate with disease.

The skilled practitioner would first turn to the instant specification for guidance and working examples to practice the claimed method of making gene panels. However, the specification does not provide such guidance or working examples. Next, the skilled practitioner would turn to the prior art for such guidance. The

> prior art shows that genes related to disease should be assessed relative to normal tissue controls. Finally, said practitioner would turn to trial and error experimentation to make and use the claimed subject matter, which represents undue experimentation.
>
> Applicant's arguments filed 17 July 2008 have been fully considered but they are not persuasive. The applicants state that meaningful information could be obtained while practicing the claimed subject matter if a benign sample was compared to a cancerous sample. The ordinary meaning of the term benign is not cancerous, and such an embodiment is not within the scope of the claimed subject matter and the argument is not persuasive. Even if, arguendo, benign tissue were considered to be cancerous, the claimed subject matter does not require one of the cancerous samples to be benign, and the scope of the claims includes embodiments in which both samples are cancerous. A review of the specification does not reveal the term benign as part of the written description at the time of filing, and it is not apparent that comparison of benign and cancerous tissues, however the applicants may intend that the samples differ, were described or enabled by the instant specification. The rejection is maintained. (Emphasis in original.)

Applicants respectfully traverse the subject rejection. As best understood by Applicants, the subject rejection appears to be predicated on the recitation in claim 1 that each of the at least two groups is cancerous. Without acquiescing in the propriety of the rejection, Applicants note that claim 1 has been amended in such a way that the language in question is no longer recited.

Therefore, the subject rejection is moot and should be withdrawn.

In addition to the above-discussed amendment to claim 1, claim 1 has also been amended to recite that steps (a) through (f) are repeated at least five times. Support for this language may be found in the present specification, for example, in the paragraph bridging pages 29 and 30.

Applicants respectfully submit that the art of record does not teach or suggest claim 1 as now presented.

In conclusion, it is respectfully submitted that the present application is now in condition for allowance. Prompt and favorable action is earnestly solicited.

If there are any fees due in connection with the filing of this paper that are not accounted for, the Examiner is authorized to charge the fees to our Deposit Account No. 11-1755. If a fee is required for an extension of time under 37 C.F.R. 1.136 that is not accounted for already, such an extension of time is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

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By: _____

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on May 18, 2009.

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Edward M. Kriegsman